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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,493	09/29/2005	Moya Caffrey	06275-471US1 101020-1P US	4620
26164 7590 07/02/2008 FISH & RICHARDSON P.C. P.O BOX 1022 MINNEAPOLIS, MN 55440-1022			EXAMINER AULAKH, CHARANJIT	
			ART UNIT 1625	PAPER NUMBER
			MAIL DATE 07/02/2008	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/551,493	<b>Applicant(s)</b> CAFFREY ET AL.	
	<b>Examiner</b> Charanjit S. Aulakh	<b>Art Unit</b> 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-14 and 17-25 is/are pending in the application.  
4a) Of the above claim(s) 23-25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-14 and 17-22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☒ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. ____.                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>8/18/06, 5/8/08</u> .   | 6) <input type="checkbox"/> Other: ____.                          |

### **DETAILED ACTION**

1. Applicant's election of group I in paper filed on May 27, 2008 is acknowledged.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse; see MPEP 818.03(a).

2. Claims 1-14 and 17-25 are pending in the application. Claims 23-25 are withdrawn from further consideration as being drawn to non-elected group.

### ***Specification***

3. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

### ***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-14 and 17-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following eight different factors (see Ex parte Foreman, 230 USPQ at 547; Wands, In re, 858.F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:

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Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on at least four of the above mentioned eight different factors such as quantity of experimentation necessary, the amount of direction or guidance provided, presence of working examples, state of the prior art, unpredictability and the breadth of claims.

In regard to lack of enablement issue of instant claims 1-14 and 17-22 for solvates of instant compounds of formula (I), there is no teaching or guidance present in the specification for preparing any specific solvates. Preparation of specific solvates of any compound is a very specialized field and involves their characterization using different techniques such as infrared spectrum, XRD powder diffraction etc. There is no teaching or guidance present in the specification regarding any specific solvents used for preparing specific solvates and their characterization using any techniques such as XRD powder diffraction or infrared spectrum etc. There is not even a single example present for preparing any specific solvate of instant compounds of formula (I). There is lot of unpredictability regarding stability of different solvates of any compound in the art. The instant compounds of formula (I) encompasses hundreds of thousands of compounds based on the values of variables R1, R2, X, Ra, Rb, Rc and Z and therefore, in absence of such teachings, guidance, presence of working examples and unpredictability, it would require undue experimentation to select specific solvates of instant compounds with enhanced stability properties.

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In regard to enablement rejection of claim 17 for methods of treatment, the specification teaches that the instant compounds are antagonists of chemokine CCR3 receptor and histamine H1 receptor in vitro ( see examples 84-86 on pages 53-55 of specification ) and also have binding affinity for histamine H1 receptor ( see example 87 on pages 55-56 of specification ). However, there is no teaching regarding antagonist activity observed at CCR3 receptors or histamine H1 receptors using these assays with any specific exemplified compound. The specification teaches on page 2 that the actions of chemokines are mediated by atleast 14 different receptors such as CCR1, CCR2 ----- CXCR4 ( see page 2, lines 8-13 ). There is no teaching or guidance present in the specification or prior art that hyperactivity of CCR3 receptors or H1 receptors is implicated in the etiology of every known disease condition mediated by activation of all these 14 different receptor subtypes of chemokines . There is no teaching in the prior art that structurally closely related compounds having antagonist activity at CCR3 receptors or H1 receptors are well known to have therapeutic utility in treating every known disease condition mediated by activation of all these 14 different receptor subtypes of chemokines. There are no working examples present showing efficacy of instant compounds in known animal models of any disease condition which is mediated by chemokines. The instant compounds of formula (I) encompasses hundreds of thousands of compounds based on the values of variables R1, R2, X, Ra, Rb, Rc and Z and therefore, in absence of such teachings, guidance, presence of working examples and prior art, it would require undue experimentation to demonstrate efficacy of instant

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compounds in known animal models of every known disease condition which is mediated by chemokines and hence their utility for treating these disorders.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 13 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 13, step b on page 7, line 2, the term ---- in presence of  $\text{NaBH}(\text{OAc})_3$  in the presence of a ---- is vague and indefinite since its actual intent is not clear.

In claim 17, specific disease conditions mediated by specific chemokine receptors are not defined.

8. Claims 1-14 and 17-22 are objected for containing non-elected subject matter.

***Allowable Subject Matter***

9. The following is a statement of reasons for the indication of allowable subject matter:

The instant compounds directed to the elected group are allowable over the prior art since they are neither disclosed nor obvious over the prior art. In the prior art, Rigby ( U.S. Patent 6,525,070, cited on applicant's form 1449 ) discloses bipiperidine derivatives which are closely related to instant compounds. However, closely related compounds of formula (Ia'') disclosed by Rigby ( see claim 5 ) differ from the instant compounds in lacking -C(O)OR<sub>b</sub> group and furthermore, there is no teaching, suggestion or motivation in the prior art to modify the compounds of Rigby to prepare the instant compounds.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571)272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Charanjit S. Aulakh/  
Primary Examiner, Art Unit 1625